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| EXAMINER | |
|---|---|
| PANDE, SUCHIRA | |
| **ART UNIT** | **PAPER NUMBER** |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/540,215 | ZIMMERMANN ET AL. | |
| | Examiner | Art Unit | |
| | Suchira Pande | 1637 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *25 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *31-61* is/are pending in the application.

4a) Of the above claim(s) *31-39 and 43-61* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☒ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/17/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

1. Applicant's election with traverse of group I invention method claims (claims 31-46 and 61) in the reply filed on May 25, 2007 is acknowledged. The traversal is on the ground(s) that Policastro et al. do not teach the sequence between 371 and 393 that is identical to SEQ ID NO 3. This is not found persuasive because Policastro et al. (1986) J Biol. Chem. 261 (13), 5907-5916 indeed does teach the sequence of SEQ ID NO. 3. Examiner had provided the alignment of the two sequences in previous Office Action. To indicate the exact region of homology Examiner has printed out the sequence of human chorionic gonadotropin beta –subunit archived in NCBI database under accession no M13505 using Pubmed. This is the accession number under which the sequence taught by Policastro et al. (1986) is archived in NCBI database. The region from nucleotide 371-393 is highlighted by Examiner. This region of chromosome 19q13.3 is 100% identical to the claimed SEQ ID No 3. A copy of Policastro et al. 1986 is also being provided with this Office Action. Therefore Examiner has properly demonstrated Lack of unity of invention hence the requirement is still deemed proper and is therefore made FINAL.

2. Applicant has elected to prosecute group I invention directed to method claims. Within that group Applicant has elected species b) claims 40-42 drawn to the method for prospective or retrospective diagnosis for implantation of an embryo for examination. Applicant's election of SEQ ID No1. and 2 as primer pair, SEQ ID No. 3 as the third primer and SEQ ID No 4 as fourth primer are acknowledged.

3. Elected species b) depends on method of claim 31, hence claim 31 is a linking claim. Consonant with the above species election, claims 32-39 and 43-61 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention. Applicant timely traversed the restriction (election) requirement in the reply filed on May 25, 2007. Claims 31 and 40-42 will be examined in this office action.

***Priority***

4. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copies filed on June 20, 2005 are in German and no English translation is provided. Hence for prior art purposes the effective filing date of the instant application is the application date of parent PCT Application No PCT/DE03/04293 filed on December 19, 2003.

***Claim Objections***

5. Elected species claim 40 recites the method according to claim 31. Since claim 40 is a method that is specifically drawn to the method for diagnosis for implantation of an embryo, Applicant is required to rewrite claim 40 in an independent form incorporating all the elements of linking claim 31. Appropriate correction is required.

***Claim Rejections - 35 USC § 112***

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 31 and 40-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 31 and 40-42 are indefinite because the claims do not recite a final process step which clearly relates back to the preamble.

Regarding claim 31, the preamble of claim 31 states " A method for determining specific conditions or changes in the endometrium or in the epithelium of other organs, the method comprising steps of: a) ---, but the final process step is the final step of claim 31 step b) which recites "quantitatively measuring in said blood sample or said tissue sample the expression or over expression of mRNA of at least one of β7-hCG, β6-hCG, and β6e-hCG". Therefore, it is unclear as to whether the claim is intended to be limited to a method of quantitatively measuring expression of mRNA of at least one of β7-hCG, β6-hCG, and β6e-hCG or a method for determining specific conditions or changes in the endometrium or in the epithelium of other organs.

Regarding claim 40, the preamble of claim 40 states that the "method according to claim 31 for prospective or retrospective diagnostic of an endometrial receptivity for implantation of an embryo, but the final process step is the final step of claim 31 step b) which recites "quantitatively measuring in said blood sample or said tissue sample the expression or over expression of mRNA of at least one of β7-hCG, β6-hCG, and β6e-hCG". Therefore, it is unclear as to whether the claim is intended to be limited to a method of quantitatively measuring expression of mRNA of at least one of β7-hCG, β6-hCG, and β6e-hCG

or a method of prospective or retrospective diagnostic of an endometrial receptivity for implantation of an embryo.

8. Claim 40-42 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01.

Currently claim 40 recites the method according to claim 31 for prospective or retrospective diagnostic of an endometrial receptivity for implantation of an embryo. But it does not recite any active step as to how this will be achieved. The omitted steps are: The step that must follow step b) of recited claim 31 so that prospective or retrospective diagnostic of an endometrial receptivity for implantation of an embryo can be performed.

Currently claim 41 recites ---- wherein, based on the determined mRNA expression of at least one of β7-hCG, β6-hCG, and β6e-hCG, conclusions in regard to receptivity of the uterus for an embryo in the actual cycle are drawn". The claim as recited does not include any active step as to how this conclusion will be drawn once mRNA expression is known.

Currently claim 42 recites---- based on determined mRNA expression of at least one of β7-hCG, β6-hCG, and β6e-hCG in the past cycle, prognoses of the potential receptivity of the uterus for an embryo in the subsequent cycle are made". The claim as recited does not include any active step as to how this conclusion will be drawn once mRNA expression is determined.

***Claim Rejections - 35 USC § 102***

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 31 and 40 are rejected under 35 U.S.C. 102(b) as being anticipated by Bellet et al. (US Pat. 6,194,154 B1 issued Feb 2001 with a PG.Pub date of September 4, 1998).

Regarding claim 31 and 40 Bellet et al teaches: the method comprising the steps of:

a) isolating RNA (see col. 5, lines 35-44 where RNA isolation is taught) from a blood sample or tissue sample (see col. 4, lines 46-53 where wide variety of tissue samples including whole blood are taught); and

b) quantitatively measuring in said blood sample or said tissue sample the expression or over expression of mRNA (see col. 4 line 4 where RT-PCR is taught for expression or over expression of mRNA for detection of CGβ transcripts) of at least one of β7-hCG, β6-hCG, and β6e-hCG (see col. 1, line 43 where β7-hCG and β6-hCG are taught).

Thus all active steps of claim 31 that are the only active steps of the recited claim 40 as currently presented are taught by Bellet et al. Hence Bellet et al. teaches all elements of claims 31 and 40.

***Claim Rejections - 35 USC § 103***

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 41 and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bellet et al. as applied to claims 31 and 40 above, and further in view of Acosta et al. (April 2000) Fertility and Sterility vol. 73, no. 4 pp 788-798.

Regarding claim 41, Bellet et al. teach method of claim 40. Bellet et al teach whole blood sample.

Regarding claim 41, Bellet et al. do not teach wherein the blood sample is taken from peripheral blood and the tissue sample is taken from tissue of endometrium or cervix of a female patient.

Regarding claim 41, Acosta et al. teach wherein the blood sample is taken from peripheral blood and the tissue sample is taken from tissue of endometrium or cervix of a female patient (see page 790 under section Menstrual cycle monitoring par. 3 where peripheral blood sampling is taught and par. 4 where endometrial biopsy sample is taught. This sample is from healthy fertile female volunteer—see page 790 section titled Volunteers par. 1). By teaching collecting endometrial tissue samples from female volunteers, Acosta et al. teach to one of ordinary skill in the art that same technique can be used to collect samples from female patient. Hence Acosta et al. teach wherein the blood sample is taken from peripheral blood and the tissue sample is taken from tissue of endometrium or cervix of a female patient.

Regarding claim 42, Acosta et al. do not specifically teach wherein the blood sample is taken from menstrual blood. However Acosta et al. do teach the method of endometrial dating and determination of the window of implantation in healthy fertile women.

It would have been prima facie obvious to one of ordinary skill in the art to practice the method Acosta et al. in the method of Bellet et al. at the time the invention was made. The motivation to do so is provided by Acosta et al. who explicitly teach endometrial dating. Also one of ordinary skill in the art knows that menstrual blood contains the cells that are shed from the uterus lining

(endometrium) if implantation of an embryo does not occur to establish a pregnancy. (see the overview section of Menstrual Cycle from free encyclopedia provided by Examiner). Thus menstrual blood is a good source of endometrial cells that have been sloughed off from the uterus. Collection of menstrual blood is non invasive, hence it would be obvious to one of ordinary skill in the art to use menstrual blood for obtaining the endometrial cells instead of using peripheral blood (an invasive collection procedure). Use of menstrual blood will result in no discomfort for the patient and will also require no specially trained technician to draw the peripheral blood resulting in a more cost effective method.

***Conclusion***

All claims under consideration 31 and 40-42 are rejected over prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suchira Pande whose telephone number is 571-272-9052. The examiner can normally be reached on 8:30 am -5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Suchira Pande
Examiner
Art Unit 1637

TERESA E. STRZELECKA, PH.D.
PRIMARY EXAMINER

Teresa Strzelecka
6/21/07